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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,883	08/07/2001	Chris Allen Broka	R0072B-REG	6198

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 07/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,883	BROKA ET AL.	
	Examiner	Art Unit	
	Binta M Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-17 and 19-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-30* is/are rejected.

7)☒ Claim(s) *1, 2, 3, 4, 5, 6, 7, -11, 13, 14, 15, 16-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The 112, first paragraph rejection of claims 1-11, 13-17, 19-36, the 112, second paragraph rejection of claim 31, 33, are withdrawn in light of applicant's amendment filed 4/23/04.

Claims 1, 2, 3, 4, 5, 6, 7, -11, 13, 14, 15, 16-26 are objected to because they contain non-elected subject matter.

The applicant's election of group II drawn to the compound of formula I, process of preparing and method of treating, wherein R1 is cycloalkyl, hydroxy, hydroxyalkyoxy, haloalkyoxy, halo, cyano, alkoxy, R2 is H, alkyl, alkenyl, alkoxy, hydroxy, halo, haloalkyl, R3 s SO2R12, R12 is alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, mono- or dialkylaminoalkyl, carboxyalkyl, or alkoxycarbonylalkyl, Ar is phenyl substituted halogen or alkoxy, A is S, O, S(O), S(O)2, -CH2, or C(=O)- noted. The Restriction is made FINAL.

(new rejections)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 28, 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating arthritis, back pain, dental pain, inflammation associated with sports injuries, ankylosing spondylitis, dysmenorrhoe or premature labor, does not reasonably provide enablement for treating synovitis, myositis, gout, headache, Alzheimer's disease, bursitis, or all cancers, inflammatory

diseases or pain in a mammal with the Cox II inhibitors claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the treatment of all inflammatory diseases, cancers, or pain in a mammal with the Cox II inhibitor compounds claimed in claim 1 and the specific diseases claimed in claims 28-29.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of all the diseases claimed, whether or not the disease is effected by the inhibition of Cox-II, is important.

It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease. (URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html). The efficacy of Cox-II inhibitors in treating synovitis, myositis, gout, pain, headache, and Alzheimer's is not well established. So far, clinical trials designed to inhibit inflammation or Cox-2 activity has failed in the treatment of Alzheimer's disease. See Ca 139:345166.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the inhibition of Cox -II, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim

1 due to the unpredictability of the role of the inhibition of Cox-II, and since the treatment of Alzheimer's disease is mediated by the breakdown of acetylcholine or the inhibition of excess amounts of glutamate. It is established I the art, however, to treat arthritis, back pain, dental pain, inflammation associated with sports injuries, ankylosing spondylitis, dysmenorrheoes or premature labor with Cox-II inhibitors. See Expert Opinion Pharmacother. (2003) 4 (2): 265-284.

The amount of direction or guidance present and the presence or absence of working examples

The only direction and guidance present in the specification are in vitro studies of Cox-I and II inhibition, in vivo studies of the anti-inflammatory activity of these compounds in rats, page 45 of the specification, and an incorporation by reference of a method for measuring the analgesic activity of these compounds in an animal model, page 47 of the specification. However, the applicant has not conducted in vivo experiments examining Cox-I and II inhibition, and in the absence of evidence to the contrary, there is no evidence that in vitro Cox-I and II inhibition study results will correlate with in vivo study results. There is no correlation between the inhibition of Cox-II and treating Alzheimer's disease or synovitis, myositis, gout, headache, Alzheimer's disease, bursitis, or all cancers, inflammatory diseases or pain in a mammal with the Cox II inhibitors claimed.

The breadth of the claims

The breadth of the claims is the treatment of all inflammatory diseases, cancers, or pain in a mammal with the Cox II inhibitor compounds claimed in claim 1 and the specific diseases claimed in claims 28-29.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited by the inhibition of Cox-II and would furthermore then have to determine which of the claimed compounds would provide treatment of the disease.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of any inflammatory disease, pain or any cancer. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of claim 27 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its

successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome deleting the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim(s) 28, 29 in part are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 28, and 29, line 1, page 5 of the amendment filed 4/23/04, the term "disease" is ambiguous because several conditions are claimed such as "back pain, dental pain, dysmenorrhoea or premature labor which are conditions and not diseases. This rejection can be overcome by changing the term "disease" to "disease or condition".

The IDS filed 12/1/03 has been considered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
July 8, 2004

JOSEPH K. McKANE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600